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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
KAM, CHIH MIN

ART UNIT	PAPER NUMBER
1653	10

DATE MAILED: 01/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/982,544	SCHULMAN ET AL.	
	Examiner	Art Unit	
	Chih-Min Kam	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 November 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) *1-12,15,19,20,24 and 26-28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13,14,16-18,21-23 and 25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group IV, claims 13-26, diabetes as the disease and thiazolidinedione as the additional active agent in Paper No. 8 is acknowledged. Regarding the selection of "one disease" and "one additional active agent", applicants presented alternative election at page 6 of the response, and examiner has used the election of a single disease and a single additional active agent for claims 13-26 based on each disease and each active agent being patentably distinct. Claims 1-12, 15, 19, 20, 24 and 26-28 are non-elected inventions, thus are withdrawn from consideration. Claims 13, 14, 16-18, 21-23 and 25 are examined.

Claim Objections

2. Claims 14, 16, 18, 23 and 25 are objected to because the claim contains recitation of non-elected diseases and additional active agents.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 13, 14, 16-18, 25 and 26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating diabetes type II comprising administering an LXR **agonist**, which is compound 1 (structure shown at page 30, paragraph 0105), or, a method of treating atherosclerotic cardiovascular diseases and related conditions such as diabetes by administering an LXR agonist having general formula $(C(R^1)(CX^1X^2X^3)(CX^4X^5X^6)(Ar\text{-}Y\text{-}R^2)$ (Shan *et al* (2001)), or an LXR agonist in combination

with a thiazolidinedione as shown in the prior art, does not reasonably provide enablement for a method for treating or preventing (not even occur at the first time) unspecified metabolic disease (in the claim) comprising administering an LXRβ selective **agonist**, or, a method for treating type II diabetes comprising administering an LXRα selective **antagonist**. The specification does not enable a person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. Shan *et al.* disclose agonists of LXR having general formula $(C(R^1)(CX^1X^2X^3)(CX^4X^5X^6)(Ar\text{-}Y\text{-}R^2))$ are used to raise high density lipoprotein (HDL) plasma level and to treat atherosclerotic cardiovascular diseases and related conditions such as diabetes by administering therapeutically amount of the compound

Claims 13, 14, 16-18, 25 and 26 encompass a method for treating or preventing a metabolic disease comprising administering an LXRβ selective agonist (claims 13, 14 and 16-18), or a method for treating type II diabetes comprising administering an LXRα selective antagonist (claims 25 and 26). The specification, however, only discloses cursory conclusions (pages 3-4) without data supporting the findings, which state that the present invention provides methods for preventing, halting or slowing the progression of metabolic diseases such as atherosclerotic cardiovascular diseases and related conditions in mammals by administering an LXRβ selective agonist, or for treating type II diabetes by administering an LXR agonist, or treating the complication of obesity such as type II diabetes by administering an LXRα selective antagonist. There are no indicia that the present application enables the full scope in view of treating or preventing a metabolic disease using an LXRβ selective agonist or an LXRα selective

antagonist. The present application provides no indicia and no teaching/guidance as to how the full scope of the claims is enabled. The factors considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F2d at 731,737, 8 USPQ2d at 1400,1404 (Fed. Cir.1988)). The factors most relevant to this rejection are the breath of the claims, the absence of working examples, the state of the prior art and relative skill of those in the art, the unpredictability of the art, the nature of the art, the amount of direction or guidance presented, and the amount of experimentation necessary.

(1). The breath of the claims:

The breath of the claims is broad and encompasses an unspecified variants regarding prevention of a metabolic disease, and the identities of LXRβ selective agonists or LXRα selective antagonists, which are not adequately described or demonstrated in the specification.

(2). The absence or presence of working examples:

There are no working examples indicating the claimed methods in association with the variants except for the use of a pan-LXR agonist, compound 1 in the treatment of type II diabetes in the mice model (pages 38-39, paragraphs 0121-0122).

(3). The state of the prior art and relative skill of those in the art:

The prior art (Shan *et al.*, WO 01/03705, Jan 2001; Piper, US 2002/0177602 A1) indicates an LXR agonist having general formula ($C(R^1)(CX^1X^2X^3)(CX^4X^5X^6)(Ar\text{-}Y\text{-}R^2)$) or a combination of an LXR agonist and a thiazolidinedione can be used to treat atherosclerotic cardiovascular diseases and related conditions such as diabetes. However, the general knowledge and level of the skill in the art do not supplement the omitted description, the specification needs to provide specific guidance on prevention of a metabolic disease, the

identities of LXRβ selective agonists or LXRα selective antagonists, and the treating conditions for various metabolic diseases to be considered enabling for variants.

(4). The amount of direction or guidance presented and the quantity of experimentation necessary:

The claims are directed to a method for treating or preventing a metabolic disease comprising administering an LXRβ selective agonist, or a method for treating type II diabetes comprising administering an LXRα selective antagonist. The specification indicates the treatment of wild type mice with a pan-LXR agonist, compound 1 results in significant increase in high density lipoprotein (HDL, paragraph 0109, Fig 5) and compound 1 can reduce hyperglycemia (elevated blood glucose) in the diabetic mice (pages 38-39, paragraphs 0121-0122, Fig. 15). However, the specification fails to identify any LXRβ selective agonist or LXRα selective antagonist, nor indicates the use of the compound in the treatment of a metabolic disease. Moreover, the specification has not shown the treating conditions for preventing a metabolic disease using the LXRβ selective agonist. There are no working examples of these methods in the specification. Furthermore, the specification does not provide any specific guidance as to how to prevent a metabolic disease, for example, the dosage, the time of the treatment and how the effect of the compound on various diseases being monitored if the disease is prevented to occur. Since the specification fails to provide sufficient guidance on the identities of LXRβ selective agonists and LXRα selective antagonists, and how to prevent a metabolic disease, it is necessary to have additional guidance and to carry out further experimentation to assess the effect of the LXRβ selective agonists and LXRα selective antagonists.

(5). Predictability or unpredictability of the art:

The claims encompass treating or preventing a metabolic disease using an LXRβ selective agonists or an LXRα selective antagonist, however, the identities of the compounds and the treating conditions for preventing metabolic diseases are not described in the specification, the invention is highly unpredictable regarding the outcome of the treatment.

(6). Nature of the Invention

Scope of the claims includes treating or preventing a metabolic disease using an LXRβ selective agonists or an LXRα selective antagonist, but the specification does not show how various disease states are being treated or prevented. Thus, the disclosure is not enabling for the reasons discussed above.

In summary, the scope of the claim is broad, while the working example does not demonstrate the claimed methods, and the guidance and the teaching in the specification is limited, therefore, it is necessary to have additional guidance and to carry out further experimentation to assess the outcome of the treatment using an LXRβ selective agonist or an LXRα selective antagonist. Thus, practice of the full scope of the presently claimed invention based upon the current claims requires the practice of undue experimentation.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 13, 14, 16-18, 21-23, 25 and 26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5. Claims 13, 14, 16-18, 21-23, 25 and 26 are indefinite because the claims lack essential steps in the method of treating a metabolic disease or diabetes. The omitted step is the outcome of the treatment. Claims 14, 16, 18, 23 and 25 are included in this rejection for being dependent on a rejected claim and not correcting the deficiency of the claim from which they depend.

6. Regarding claims 14 and 18, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

7. Claims 21 and 22 are rejected under 35 U.S.C. 102(a) as being anticipated by Shan *et al.* (WO 01/03705, Jan 2001).

Shan *et al.* disclose agonists of LXR having general formula $(C(R^1)(CX^1X^2X^3)(CX^4X^5X^6)(Ar\text{-}Y\text{-}R^2))$ are used to raise high density lipoprotein (HDL) plasma level and to treat atherosclerotic cardiovascular diseases and related conditions such as diabetes by administering therapeutically amount of the compound (page 2, line 28-page 4, line 14, page 25, lines 1-7; claims 21 and 22).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 21-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shan *et al.* (WO 01/03705, Jan 2001) taken with Piper (US 2002/0177602 A1).

Shan *et al.* disclose agonists of LXR having general formula $(C(R^1)(CX^1X^2X^3)(CX^4X^5X^6)(Ar\text{-}Y\text{-}R^2))$ are used to raise high density lipoprotein (HDL) plasma level and to treat atherosclerotic cardiovascular diseases and related conditions such as diabetes by administering therapeutically amount of the agent (page 2, line 28-page 4, line 14, page 25, lines 1-7; claims 21 and 22). The reference also teaches an LXR agonist can be administered with an active agent (pages 27-28). However, Shan *et al.* do not disclose the use of a thiazolidinedione as the additional active agent in combination with an LXR agonist for the treatment. Piper teaches the use of a thiazolidinedione oral antidiabetic agent in combination

with metformin for treating type II diabetes in combination therapy (paragraph 0062). At the time the invention was made, it would have been obvious to one of ordinary skill in the art to treat diabetes using the method taught by Shan *et al.* in combination with a thiazolidinedione taught by Piper because the use of an active agent in addition to the LXR agonist would allow the use of lower dose of the compound which would have reduced side effects (paragraph 0030). Thus, the combined references result in the claimed invention and was, as a whole, prima facie obvious at the time the claimed invention was made.

Conclusion

9. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (703) 308-9437. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (703) 308-2923. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-0294 for regular communications and (703) 308-4227 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Chih-Min Kam, Ph. D. CMK
Patent Examiner

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January 23, 2003

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